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Leukaemia Section
Short Communication

t(9;10)(q34;q22) ZMIZ1/ABL1

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Abstract

Short communication on t(9;10)(q34;q22) ZMIZ1/ABL1, with data on clinics, and the genes implicated.

Clinics and pathology

Note
Only five cases to date have been described with a t(9;10)(q34;q22).
Two cases of acute myeloid leukemia (AML) are herein excluded from the study, because they are likely to represent another entity, with perhaps different genes involved.
These are two patients aged 44 years (1 female and 1 male), one with a M1-AML, and the other one with a M3-AML and the classical t(15;17)(q22;q21), both with a complex karyotype and no further data (Sato et al., 1995; Schoch et al., 1996).

Disease

B-cell acute lymphoblastic leukemia (B-ALL).

Phenotype/cell stem origin

One case was phenotyped as a CD10+ B-ALL.

Epidemiology

Three cases to date, 1 male / 2 female patients, all are paediatric cases so far, one was a 1.5 year old baby (Cooley et al., 2007; Rabin et al., 2008; Soler et al., 2008).

Prognosis

Scarce data, no follow-up; one case was noted as being in complete remission.

Cytogenetics

Cytogenetics morphological

Additional abnormalities were found in the three cases (complex karyotype in two cases). A del(13q) was found in one case.

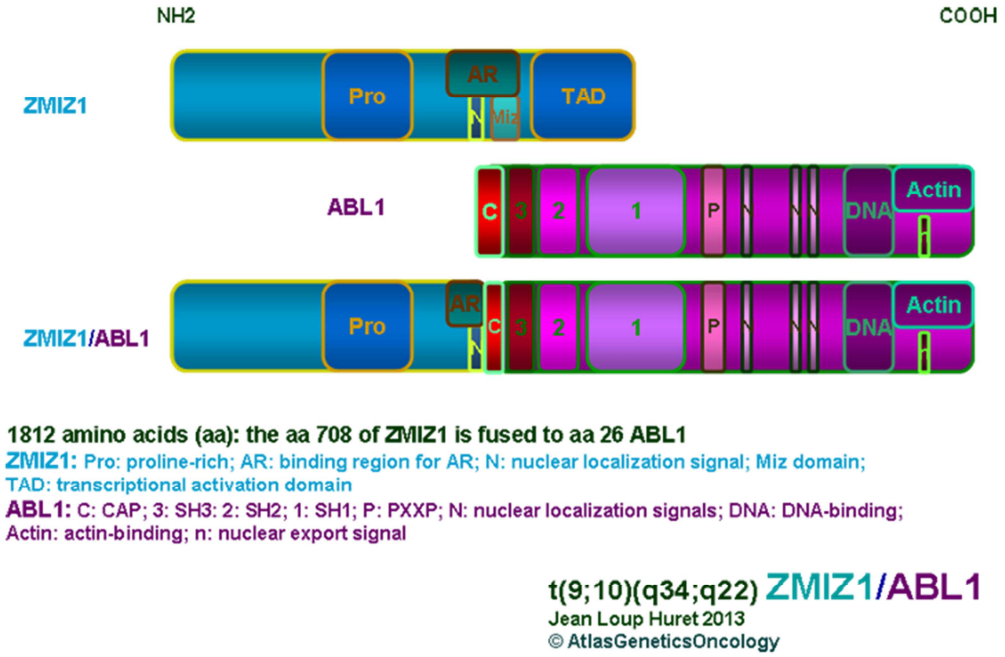
Genes involved and proteins

ABL1

Location
9q34.12

Protein
1130-1143 amino acids; ABL1 is composed from N-term to C-term of a CAP, a SRC homology 3 (SH3), SH2 and SH1 tyrosine kinase domains, a conserved PXXP motifs to mediate protein-protein interactions, three nuclear localization signal (NLS) motifs, a DNA-binding domain, a globular (G).actin-binding domain, one nuclear export signal (NES), and a conserved filamentous actin-binding domain. Regulates endocytosis, epithelial-to.mesenchymal transition, cell polarity, adhesion, migration and invasion; in response to cellular stress, including DNA damage, ABL1 induces growth arrest and/or apoptosis (review in Greuber et al., 2013).

Somatic mutations
Apart from the well known role of ABL1 in leukemias, ABL1 has been found overexpressed in a small percentage of breast carcinomas, lung squamous cell carcinomas, and uterine corpus carcinomas.



t(9;10)(q34;q22) ZMIZ1/ABL1 protein.

ZMIZ1

Location
10q22.3

Protein
1067 amino acids (aa). ZMIZ1 is composed from N-term to C-term of a proline-rich region (aa 363-555 (334-555 according to Swiss-Prot)), a nuclear localization signal sequence (aa 691-713), a Miz domain (aa 738-790 (Zn finger 727-804 according to Swiss-Prot)), and a proline-rich region (transcriptional activation domain) (aa 824-1067 ((867-1002 according to Swiss-Prot)).
The central region between aa 556 and 790 is the primary binding region for AR (Sharma et al., 2003). Sequence specific DNA binding protein. Transcriptional coactivator related to members of the proteatggactin inhibitor of activated STAT (PIAS) family.
Co-activator of AR (androgen receptor).
Increases ligand-dependent transcriptional activity of AR, SMAD3, and TP53. ZMIZ1 is able to enhance the sumoylation of AR.
ZMIZ1 cooperates with NOTCH1 to regulate the C-MYC pathway.
ZMIZ1 is overexpressed in a subset of T-ALL (Rakowski et al., 2013).

Result of the chromosomal anomaly

Hybrid gene

Note
A ZMIZ1/ABL1 hybrid gene was searched for and detected in one case to date (Soler et al., 2003).

Description
5' ZMIZ1-3'ABL1. The exon 14 of ZMIZ1 is fused to exon 2 of ABL1.

Fusion protein

Description
197 kDa, 1812 amino acids fusion protein, containing the N-term proline-rich domain of ZMIZ1 and most of ABL1.

Oncogenesis
ZMIZ1/ABL1 may encode a constitutively activated tyrosine kinase.

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